

### REMARKS

Applicant's attorney would like to thank the Examiner for the careful consideration given to this case. In light of the remarks presented *vide infra*, it is respectfully submitted that the claims are now in condition for allowance and notice to such effect is requested.

Claims 1-38 stand rejected under 35 U.S.C 103(a) as being unpatentable over a U.S. Patent No. 6,114,038, ('038), to Castro et. al in view of a reference to Korgel et. al. J. Phys. Chem. **1996**, 100, 346-351 ("Korgel"). It is the Examiner's position that the present claims would be obvious in view of Castro's teaching of functionalized fluorescent nanocrystals, method of preparation, and uses thereof, in view of Korgel's purported teaching of using liposomes such as phosphatidylcholine to grow fluorescent nanocrystals. It is respectfully submitted that the Examiner has not considered the respective claim groups or the art. The examiner has not considered the invention as a whole in view of the teachings of the art.

The Castro et. al '038 patent discloses water-soluble functionalized nanocrystals comprising pre-formed nanocrystals capped with a bonded mercaptoalkylcarboxylic acid operably linked to a diaminocarboxylic acid. The diaminocarboxylic acid may be further operably linked to an affinity ligand or to an amino acid which itself is bonded to an affinity ligand. Functionalized nanocrystals with operably bound affinity ligands may be used to detect the presence or absence of a target substrate. This reference discloses operably bonding functional groups in a sequential fashion to the semiconductor nanocrystal.

Korgel et. al. disclose the use of "size-monodisperse" phosphatidylcholine vesicles to grow size-monodisperse (mean diameter  $\pm 8\%$ ) crystalline CdS nanoparticles. The reference method discloses the formation of size-monodisperse phosphatidylcholine vesicles containing  $\text{Cd}^{+2}$ . The vesicles containing  $\text{Cd}^{+2}$  are formed by dialysis of a detergent/lipid micelle dispersion. These vesicles containing  $\text{Cd}^{+2}$  are used for *growing* fluorescent nanocrystals within the liposomes by treatment with ammonium sulfide. The size of the nanocrystal formed by the method of this reference is very sensitive to the vesicle diameter which is itself is very sensitive to  $\text{CdCl}_2$  concentration and detergent dialysis rate.

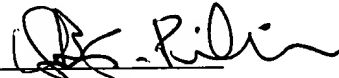
Applicant's instant invention discloses the encapsulation of fluorescent nanocrystals into liposomes and the functionalization of such liposomes. It is the reference of Korgel, and not the applicant, who makes the statement that "Growth of nanocrystals in surfactant bilayers vesicles (e.g. liposomes) may provide a more rationally based method to produce particles of predetermined size, shape, and crystallinity." The reference discloses the *growth* (emphasis added) of nanocrystals but does not disclose the desirability of functionalizing liposomes.

It is respectfully submitted that a *prima facie* case of obviousness has not been established. There is no motivation or suggestion to look to Korgel as suggested by the Examiner. The Examiner's statement regarding the alleged obviousness of the Applicant's instant invention in view of the references is not appropriate for rejection under 35 U.S.C. 103 absent the Examiner qualifying himself/herself as a particular expert in this field. The Examiner is respectfully referred to 37 C.F.R. § 1.104(d)(2) for the general requirement to base a rejection on documentary prior art or via an affidavit by the Examiner (also see MPEP § 2144.03). Even assuming *arguendo* that the Examiner's statements are documented, there is no motivation provided by any reference to arrive at Applicant's instant invention. Absent such motivation or suggestion it is improper to combine the references in support of a obviousness rejection under U.S.C. § 103. The Federal Circuit, in a recent case, *In re Roufet*, (see also MPEP § 2144.01), reversed an obviousness rejection where, as in this case, the Examiner improperly pieced together elements in the prior art when there was no motivation to do so.

It is respectfully submitted that the Examiner is piecing together elements of the prior art to arrive at the Applicant's invention. This is improper hindsight. Only when armed with the Applicant's disclosure would one arrive at the aspect of functionalizing liposome encapsulated nanocrystals. The Examiners's rejection of claims 1-38 is hindsight based upon Applicant's disclosure and therefore should be withdrawn.

In view of the remarks presented above, it is believed that pending claims 1-38 are in condition for allowance and notice to such effect is respectfully requested. Although Applicant believes no fees are due, the Commissioner is hereby authorized to charge my deposit account No. 50-0436 for any fees that may be due in connection with this response. Should the Examiner have any questions regarding these remarks, the Examiner is invited to initiate a telephone conference with the undersigned.

Respectfully Submitted,



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Dated: February 21, 2003